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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/591,632	06/09/2000	Susan Lindquist	27373/34978A	2820

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EXAMINER	
BRANNOCK, MICHAEL T	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/591,632	LINDQUIST ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2003*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *60,61,65,67,81,101-114 and 116-143* is/are pending in the application.

4a) Of the above claim(s) *60,61 and 111-114* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *65,67,81,101-110,116 and 119-143* is/are rejected.

7)☐ Claim(s) *117 and 118* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/27/03 has been entered.

Response to Amendment

Claims 60, 61, 111-114 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14, 5/13/02.

Applicant is reminded that the claims are under examination only to the extent that they read on the elected invention, i.e. polypeptides having a reactive SCHAG amino acid sequence, comprising SEQ ID NO: 2 or a fragment thereof, a modified cysteine residue, and a metal atom substituent.

Maintained Rejections:

Claims 65, 67, 101, 119, 120, 139 and 141 stand rejected under 35 U.S.C. 102(b) as being anticipated by Gregori et al., J. Biol. Chem. 272:1(58(62)1997, as set forth previously and reiterated below.

Gregori et al. disclose a polypeptide comprising a self-aggregation domain of Amyloid-protein (residues 1-40, as is well known in the art) comprising the substitution of residue 40 with a cysteine residue having a reactable side chain and further modified with a metal ion (gold), see

col 1 of page 59. Gregori et al. further disclose that the labeled peptide forms ordered aggregates see col 1 of page 60, therefore one of ordinary skill in the art would expect that the gold labeled side chain is exposed to the environment in an ordered aggregate because the gold does not appear to inhibit aggregation as would be expected if the gold was buried in the interior of the aggregate.

Applicant argues that Gregori et al. failed to disclose that the labeled peptide formed ordered aggregates and contains teachings that suggest that it did not. Specifically, Applicant argues that Figure 2 does not support evidence for aggregation and that the term "complex", as stated in the figure legend refers to a complex consisting of the Aβ and nanogold particle and not to a multimeric complex of such. Applicant's arguments are persuasive. A more careful reading of this figure and of Figure 1 indicate that under these conditions higher ordered Aβ structures would not be expected to form, see Figure 1A first lane wherein wild type Aβ appears as a single intense band at the bottom of the gel. As set forth in the text of Gregori et al., wild type Aβ rapidly aggregates at concentrations higher than 200 μM; such conditions were presumably not used here. Furthermore, Figure 2A is that of a gel run under denaturing conditions, thus even if $A\beta^{Au}$ were to form aggregates these aggregates would be expected to dissolve due to denaturation of the protein.

As set forth in the Prior Office action, evidence that the $A\beta^{Au}$ forms aggregates appears in col 1 of page 60. Each of Applicant's arguments appearing in the Remarks section of the response will be answered in parallel with the arguments presented in the accompanying Declaration filed 10/27/03. In item 2.7 of the Declaration, Applicant argues that the property of aggregation as discussed by Gregori refers to wild type Aβ and not to the gold labeled Aβ which Gregori refers to as $A\beta^{Au}$. This argument has been fully considered but not deemed persuasive.

Unfortunately for the purpose of this discussion, Gregori has not been consistent in the reference to $A\beta^{Au}$. Gregori variously refers to $A\beta^{Au}$ as $A\beta^{Au}$ or $A\beta$. For instance, in col 1 of page 61, Gregori writes "As Fig. 4D indicates, $A\beta$ did not randomly bind the proteasome, but there appeared to be two well defined regions of preferential binding". In this sentence Gregori is clearly referring to $A\beta^{Au}$ which was used in the experiment, see the figure legend, and not to wild type $A\beta$, yet Gregori use the term $A\beta$ instead of $A\beta^{Au}$. Thus, these terms can often be used interchangeably. Returning to col 1 of page 60, the third full paragraph refers to the analysis of $A\beta^{Au}$ inhibition of ubiquitin-dependent degradation, yet Gregori states that "As already discussed, no further kinetic analysis could be performed due to the anomalous behavior of $A\beta$ in solution". Gregori is clearly referring to the fact that additional analysis of $A\beta^{Au}$ could not be performed because $A\beta^{Au}$, like the wild-type $A\beta$, has the "anomalous" behavior of self-aggregating at concentrations high enough to determine saturation binding, see the first full paragraph of col 1 page 60. Additionally, it is difficult to reconcile Applicant's line of argument with the statement in item 2.9 of the Declaration that "Gregori also teaches that the 1.4 nm Nanogold particle caused 'anomalous behavior of $A\beta$ in solution'". The actual sentence from Gregori deserves repeating "As already discussed, no further kinetic analysis could be performed due to the anomalous behavior of $A\beta$ in solution". As, discussed above the term $A\beta$ is used, yet item 2.9 of the Declaration asserts that Gregori is referring $A\beta^{Au}$ whereas item 2.7 asserts that Gregori only refer to $A\beta^{Au}$ using the term "$A\beta^{Au}$" and not $A\beta$. Applicant cannot have it both ways. One of ordinary skill in the art appreciates that this sentence directly refers to $A\beta^{Au}$ and that $A\beta^{Au}$ shares the same anomalous properties in solution as wild type.

In item 2.9 of the Declaration, Dr. Linquist speculates that the Nanogold moiety is substantial in size compared to the size of the Aβ peptide, representing perhaps 70% or more of the total size (using the molecular weight markers and migration patterns of free Nanogold and Aβ as the criteria from Figure 2A), and because of this tremendous size difference Dr. Linquist asserts that steric hindrance of the gold particle would be expected to inhibit aggregation. This argument has been fully considered but not deemed persuasive. First, the examiner does not understand how the behavior of a gold particle in an SDS-PAGE gel could provide any information as to the real molecular weight or the size of the gold particle. Regardless, we already know what the size is; it is 1.4 nm in diameter, as is readily stated in the Declaration and in Gregori et al. 1.4 nm is approximately the length of a small peptide having five amino acids, see Figure 3-30 on page 114 of Alberts ed. Molecular Biology of the Cell. The Aβ peptide is 40 amino acids in length. One would expect that the gold would not inhibit self aggregation because it did not inhibit proteasome binding and displayed the same "anomalous behavior" in solution as wild type, i.e. it self aggregates, as taught by Gregori. Further, it is unclear if Dr. Linquist is actually asserting that she believes that the labeled Gregori peptide would not form higher ordered aggregates. One can only infer from her statement that she does not believe or predict that they would form higher ordered aggregates "as contemplated in the patent application". What bearing this phrase has in relation to the instant claims cannot be discerned.

Additionally, Applicant's reasonings are difficult to reconcile with the disclosure of the instant application wherein the assertion has been made that Aβ could be used as a fusion with GFP, see page 50; GFP having a molecular weight of 26 kDa, which would make the GDP portion approximately 80% of the total size of the protein.

Applicant argues that several claims require that the polypeptide form various polymers and that there is no teaching or suggestion in Gregori the peptide has these properties. This argument has been fully considered but not deemed persuasive. In each experiment conducted by Gregori, the labeled peptide had properties similar to the wild type. Thus, if it is agreed that the wild type peptide forms these polymers, then the labeled peptide would be expected to, absent evidence to the contrary.

Applicant argues that the proteasome/$A\beta^{Au}$ complex was shown not to form polymers. This argument has been fully considered but not deemed persuasive. The examiner can think of no reason why it would and nor does he understand the relevance of this to the instant rejection.

Claim Rejections - 35 USC § 103

Claims 102-110, 116, 119-122, 124, 125, 126, 132, 134, 135, 137-140, 142, 143 stand rejected under 35 U.S.C. 103(a) as being unpatentable over King et al. PNAS 94(6618-6622)1997 in view of Gregori et al., J. Biol. Chem. 272:1(58(62)1997, as set forth previously.

Applicant's arguments regarding this rejection have been addressed previously and above as the arguments relate to the teachings of Gregori et al.

Claims 65, 67, 81, 101, 119, 120, 139-141 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No: 5750361 in view of Stayton et al. J. Biol. Chem. 263(27)1344-13548, 1988, as set forth previously and reiterated below.

U.S. Patent No: 5750361 discloses methods of assaying formation of prion complexes (i.e. SCHAG amino acid sequences) by constructing polypeptides comprising prion aggregation domains labeled using materials and methods well known in the art including florescent dye and spectrophotometrically-detectable chromophores (see col 11 bridging col 12). U.S. Patent No: 5750361 discloses assays to determine that the labeling occurs at positions exposed to the environment, i.e. that the label does not interfere with complex formation (e.g. col 11 and 12). U.S. Patent No: 5750361 does not specifically recite that the act of labeling the polypeptide include the steps of choosing an amino acid residue in the sequence having a side chain that is exposed to the environment and substituting this amino acid with one having a reactive side chain; however these steps are old and well established to in the art of protein complex detection. For example, Stayton et al. disclose a method of labeling a polypeptide comprising identifying residues having side chains exposed to the environment (Threonine at positions 6 and 68 of Cytochrome b5) and substituting these residues with residues having a reactive side-chain and further modifying the reactive side chains with a fluorescent agent (see the Abstract and col 2 of page 13544). U.S. Patent No: 5750361 also disclose that the polypeptides can be further modified to accept a biotin group through methods well known in the art, e.g. derivation of a reactive lysine side chain (see col 12, L27-39).

Additionally, claim 140 requires that the fibrous polymer be attached to a solid support. U.S. Patent No: 5750361 discloses that the modified peptides be attached to a solid support, e.g. col 11, lines 48-50.

Therefore, it would have been obvious to one of ordinary skill in the art, with reasonable expectation of success, to produce a polypeptide comprising a prion aggregation domain for use

in an assay to detect prion aggregates (and thus producing the aggregates themselves) labeled with a fluorescent or other spectrophotometrically-detectable substituent, and also a lysine residue for biotinylation, as taught by U.S. Patent No: 5750361 and to accomplish this by selecting a residue having a side chain exposed to the environment and replacing that residue with one having a reactable side chain and then further modifying the side chain with a fluorescent dye, as taught by Stayton et al. and/or a biotin molecule as is old in the art. The motivation to do so was provided by U.S. Patent No: 5750361 wherein it is stated that the polypeptide should be modified as described in the art and that amino acids could be substituted as long as the change does not effect complex formation (col 7, L30-36) and by Stayton et al who provide methods of labeling a polypeptide, wherein the labeled polypeptide is useful for detection of complex formation.

In items 3.3-3.5 of the Declaration and on pages 12-13 of Applicant's remarks, Applicant argues that the techniques used by Stayton would not be amenable to use with prions because Stayton's techniques relied on having the crystallographic structure of the protein, and no such data are available for prions. This argument has been fully considered but not deemed persuasive. Stayton is being relied upon only to demonstrate the concept, that is widely appreciated in the art, that if one wishes to study protein/protein interactions using the various available labeling techniques, then one would be motivated to modified residues that are exposed to the environment when the protein complexes are formed, and that this can be accomplished by replacing that residue with one having a reactable side chain and then further modifying the side chain with a fluorescent dye. This is a very simple concept and is obvious to anyone skilled in the art. It is well appreciated that there are two simple reasons for this: (a) that modification of

residues buried in the interior of the complex would be more likely to affect the conformational stability of the complex, and (b) if the reporter conjugate is buried in the interior of the complex, then the signal emanating from that conjugate is likely to be diminished. Methods for determining what residues are exposed to the environment are well known in the art, as is essentially admitted to in the instant specification, e.g. scanning mutagenesis assays and computational predictions (see pages 23-25). U.S. Patent No: 5750361 discloses assays to determine that the labeling occurs at positions exposed to the environment, i.e. that the label does not interfere with complex formation (e.g. col 11 and 12). The specification adds nothing more in that regard. If Applicant is arguing form the stand-point, that one of ordinary skill in the art would not know how to find residues exposed to the environment in a prion complex, then it is difficult to understand how Applicant's claims would be enabled because the specification has simply reiterated what is art standard. Again, the issue regarding the Stayton reference is that it explicitly teaches the desirability of modifying residues that are exposed to the environment when studying protein/protein interactions, as is well established and old in the art.

In item 3.8 and on page 13 of the Remarks, Applicant argues, essentially, that a person of ordinary skill, would not be motivated to alter the teachings of Pursiner to arrive at the instant invention because Pursiner is interested in finding compounds that inhibit complex formation whereas, in stark contrast, the instant application concerns using labels that do not inhibit complex formation. This argument has been fully considered but not deemed persuasive, although the examiner admits that he may not understand the basis of the argument. One of ordinary skill in the art appreciates that in order to find compounds that inhibit complex formation, one must have an assay that allows for complex formation, otherwise one would

never know that a compound has inhibited complex formation. Thus, Pursiner is interested in labeling the proteins in such a way that does not interfere with complex formation, so that molecules can be tested for the ability to disrupt complex formation.

In items 3.9-3.12 of the declaration and on page 13 of the Remarks, Applicant argues, essentially, that Prusiner's assay can be practiced with unaltered PrP protein, including labeling with fluorescent dies, etc. and that combining Pursiner and Stayton is a slow and expensive process requiring crystallization. This argument has been fully considered but not deemed persuasive. As set forth above, one would not need crystallization to find residues that are exposed to the environment to take advantage of this concept as exemplified by Stayton, i.e. when labeling the peptide one simply determines that the labeled residues do not inhibit complex formation as taught in the Prusiner patent, e.g. col 11 and 12. Furthermore, as has been discussed, one of ordinary skill in the art appreciates that adding a label is equivalent to altering the primary sequence of the protein because the label completely changes the chemical nature of the residue to which it has been added. This problem is compensated for by choosing sites in the peptide that are exposed to the environment when the complex has formed – a way to selectively label such sites is to mutate the residue to one that can be selectively labeled (as taught by Stayton).

In item 3.12 of the Declaration, Applicant asserts that the only variant contemplated by Prusiner is one that causes disease, and the desirability of other variants is not taught. This argument has been fully considered but not deemed persuasive. Prusiner mentions this variant only as an example, see line 38 of col 7. Pursiner teach the general applicability of making variants and testing them to confirm their prion-forming properties. This teaching in

combination with that of Stayton who teaches that labels can be added to specific residues buy mutating those residues to specifically accept that label, provides the motivation and the teaching of the desirability and expectation for success to mutate the primary sequence so as to specifically add a label.

Claims 102-109, 116, 121-126 and 132 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No: 5750361 in view of Stayton et al. J. Biol. Chem. 263(27)1344-13548, 1988 and in further view of King et al. PNAS 94(6618-6622)1997, as set forth previously, Applicant's arguments are discussed above.

Claims 127-131 and 133-138 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No: 5750361 in view of Stayton et al. J. Biol. Chem. 263(27)1344-13548, 1988 and King et al. PNAS 94(6618-6622)1997 as set forth above regarding claims 102-109, 116, 121-126, and in further view of Paushkin et al., Science 277(381-383)1997, as set forth previously. Applicant's arguments are discussed above.

Claim Rejections - 35 USC § 112

Claims 124, 127-131, 134-137 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, as set forth previously and reiterated below.

The specification discloses a polypeptide of SEQ ID NO: 2, yet the claims require an essentially limitless number polypeptides having only 90% identity with SEQ ID NO: 2, e.g. sequences from other species, artificially mutated sequences and allelic variants. None of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that many of these proteins would work as required by the claims, one would not be able make useful predictions as to the amino acid positions or identities of those sequences based on the information disclosed in the specification.

The instant disclosure of a single polypeptide, that of the naturally occurring SEQ ID NO: 2, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polypeptide sequence SEQ ID NO: 2, which is not sufficient to describe the essentially limitless genera encompassed by the claims.

Thus, with the exception of the of the polypeptide of SEQ ID NO: 2, the skilled artisan cannot envision encompassed variants. Therefore, only a polypeptide of SEQ ID NO: 2, and polypeptides *consisting* of fragments thereof, or polypeptides consisting of fragments thereof and heterologous sequences (e.g. carrier or tag sequences), but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant argues that the claims are limited to a defined sequence similarity and a defined functional property that the specification has clearly provided methods of identifying such variants. This argument has been fully considered but not deemed persuasive. The claims encompass a vast genus of polypeptides that were not described in the specification; and nor could an artisan accept that Applicant was in possession of such a genus based on the disclosure. The simple recitation of a percent identity in no way describes any particular polypeptide. It does not describe any particular structure or function. Similarly, simply verbalizing or putting in writing that a polypeptide variant should have a particular function in no way places such a variant in one's possession.

Applicant argues that Example 14 of the Written Description Guidelines provides that recitation of percent identify in combination with a functional limitation to a genus is an accepted method of describing and claiming a genus. This argument has been fully considered but not deemed persuasive. As set forth above, simply verbalizing that a polypeptide should have some function does not put one in possession of such a peptide. Applicant is reminded that Example 14 includes an important fact in the pattern that is not present here. In Example 14, "procedures for making variants of SEQ ID NO: 3 which have 95% identity to SEQ ID NO: 3 and retain its activity are conventional in the art." There does not appear to be any conventional art-recognized procedures that produce variants of SEQ ID NO: 2 that are 90% identical to SEQ ID NO: 2 and yet retain the ability to self-coalesce.

New Rejection:

Claim 81 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 81 has been amended to require the isolated polypeptide have exactly 2 selectively reactable side chains. Thus the SHAG polypeptide cannot have less than 2 and it cannot have more than 2. The specification sets forth that cysteine, lysine, tyrosine, glutamate, aspartate, and arginine possess reactable side chains (e.g. page 24). There appears to be no description of a SHAG polypeptide with the required functional properties that does not include more than 2 of the above recited amino acids.

Conclusion

Claims 117 and 118 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

This application contains claims drawn to an invention nonelected with traverse in Paper No. 14. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art

of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Please note the new official fax number below:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Thursdays from 8:00 a.m. to 5:30 p.m. The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

January 4, 2004

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600